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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/827,106	04/19/2004	Gopi M. Venkatesh	EURA-008/00US 307853-2228	1448

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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	**PAPER NUMBER**
1618	

NOTIFICATION DATE	DELIVERY MODE
05/12/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

zpatdcdocketing@cooley.com

Office Action Summary	Application No.	Applicant(s)	
	10/827,106	VENKATESH ET AL.	
	Examiner	Art Unit	
	JAGADISHWAR SAMALA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Amendments and Request for Continued Examination filed on 01/19/2011.

- Claim 1 has been amended.
- Claims 1-15 are pending and presented for examination.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/19/2011 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "not more than about" and also "not less than about" in claims 1-6 is a relative term which renders the claim indefinite. The term "about" is not defined by the

claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gowan (US 5,876,759)in view of Ohta Motohiro et al (EP 914818 A1) and Guo et al (US 2004/0068000 A1).

Applicant's claims are drawn to a tablet that rapidly disintegrates in the oral cavity comprising a compressed blend of: rapidly dispersing microgranules consisting essentially of sugar alcohol, and taste-masked microcapusles containing at least one

drug and at least one polymeric binder, wet milling the granulated mass, and microencapsulating the milled granules to provide microcapsules.

Gowan discloses a rapidly disintegrating pharmaceutical dosage form (tablet) containing coated pharmaceutical particles with a taste-masking composition comprising a water-disintegratable, carbohydrate, and a binder and a process for preparing such dosage forms (col. 2 lines 27-32). Pharmaceutical actives include famotidine, ranitidine, cimietidine mixtures thereof (col. 6 lines 28-37), water-disintegratable carbohydrates include mannitol, sorbitol, dextrose, sucrose, xylitol, lactose, and mixtures thereof (col. 3 lines 23-25); binders include cellulosic derivatives, polyvinyl pyrrolidone, starch, modified starch (col. 3 lines 32-36). The coated particle refers to solid pharmaceutical actives in the form of a crystal or particle, an agglomerate of individual particles or a granuled particle which would read on microencapsulating the microgranules to provide microcapsules. The coated pharmaceutical particles have particle size generally less than 400 microns and disintegrates in the mouth within about 30 seconds (col. 7 lines 32-34). Additional disclosure includes dosage forms upon administration; coated pharmaceutical particles are released from the dosage form with no objectionable taste and swallowed by the user (col. 3 lines 5-8).

Gowan does not teach separately granulating a sugar alcohol or a saccharide or a mixture thereof having an average particle size less than about 30 micron to provide rapidly dispersing microgranules and drug sumatripan.

Ohta discloses a method of preparing a rapidly disintegrating tablet comprising sugar alcohol or saccharide having an average particle diameter of not more than 30

microns, an active ingredient, and a disintegrant (see 0004).The tablet can be obtained by compressing and tableting after granulating a mixed powdered component comprising sugar alcohol such as D-mannitol or saccharide ground by means of a hammer mill or a jet mill or the like (see 0018). The disintegrant mainly used such as crospovindone, crosscarmellose sodium, low substituted hydroxypropylcellulose or the like which is widely used for drugs and food (see 0016). The amount of sugar alcohol or saccharide is preferably about 60-95 % by weight of tablet (see 006 and 0019).The amount of active ingredient for e.g. cimetidine is 0.01-10 %, and the amount of disintegrant present is preferably about 1-30mg per dosage, and more preferably 1- 10 % per one tablet (see 0021).

Guo discloses a pharmaceutical composition of a compression coated tablet comprising a tablet core containing an effective amount of a bitter or unpleasant tasting pharmaceutically active agent such as sumatripan and a compression coat on the tablet core (abstract and 0023). And core composition comprise a disintegrant, crospovidone (0009), binders include starch, polyvinylpyrrolidone or hydroxypropylmethylcellulose (0012), fillers like lactose, sorbitol, mannitol and the like (0010). Additional disclosure includes that the oral dosage form, sumatriptan's unpleasant taste and smell may exacerbrate the nausea and vomiting associated with migraine is reduced by formulating dosage form as a tablet, which is compression coated by non-interacting materials thereby eliminating the bitter taste and unpleasant smell of the active pharmaceutical ingredient (0004).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate sugar alcohol or saccharide, such as D-mannitol or lactose having an average particle diameter of not more than 30 microns into the tablets as taught by Gowan to reduce the undesirable taste or bitterness of the pharmaceutical and providing with a pleasant taste perception. The person of ordinary skill in the art would have been motivated to make these modification, because Gowan teaches, that coated pharmaceutical particles with a taste-masking composition comprising a water-disintegratable carbohydrate, and a binder upon administration are released from the dosage form with no objectionable taste and swallowed by the user, which could improve the patient's compliance and acceptance with the drug regime and reasonably would have expected success because both Gowan and Ohta teaches a rapidly disintegrating tablet that can be used in the same field of endeavor such as taste-masking rapidly disintegrable tablets which does not require a special pharmaceutical manufacturing technology and can be simply and easily produced by a normal equipment.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate sumatriptan drug into Gowan's pharmaceutical dosage form. The person of ordinary skill in the art would have been motivated to make those modifications because Guo teaches that the bitter active agent such as sumatriptan when covered with compression-coated by non-interacting materials such as microcrystalline cellulose, lactose, mannitol, sorbitol... (0007 and 0016), provides elimination of the bitter taste and unpleasant smell of the active pharmaceutical

ingredient and reasonably would have expected success because both Gowan and Guo teaches a pharmaceutical dosage forms that can be used in the same field of endeavor such coated taste masked solid dosage forms (tablets).

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gowan (US 5,876,759)in view of Ohta Motohiro et al (EP 914818 A1) and Guo et al (US 2004/0068000 A1) as applied to claims 1-2 and 4-15 above, and further in view of Ryde et al (US 2002/0110597).

Claims are drawn to a tablet that rapidly disintegrates in the oral cavity comprising a compressed blend of: rapidly dispersing microgranules consisting essentially of sugar alcohol, and taste-masked microcapusles containing at least one drug and at least one polymeric binder, wet milling the granulated mass, and microencapsulating the milled granules to provide microcapsules, wherein granulating formulation comprising at least one drug with an average particle size of not more than about 50 microns, at least on binder, and optionally a diluent(s) and a disintegrant, said microgranule exhibiting not more than 15% fines.

Gowan discloses a rapidly disintegrating pharmaceutical dosage form (tablet) containing coated pharmaceutical particles with a taste-masking composition comprising a water-disintegratable, carbohydrate, and a binder and a process for preparing such dosage forms (col. 2 lines 27-32). Ohta discloses a method of preparing a rapidly disintegrating tablet comprising sugar alcohol or saccharide having an average particle diameter of not more than 30 microns, an active ingredient, and a disintegrant (see 0004).The tablet can be obtained by compressing and tableting after granulating a

mixed powdered component comprising sugar alcohol such as D-mannitol or saccharide ground by means of a hammer mill or a jet mill or the like (see 0018). The skilled artisan at the time the invention would have understood from the teachings of Gowan and Ohta that conventional techniques was compatible with rapidly disintegrating taste-mask pharmaceutical dosage form (tablet) including histamine H1 receptor antagonists. Both Gowan and Ohta teaches conventional tableting machines to compress the ingredients into the final dosage form with no objectionable taste and swallowed by the user.

Gowan and Ohta do not teach the specific drug with an average particle size of not more than about 50 microns and said microgranules exhibiting not more than 15% fines.

Ryde teaches solid dose nanoparticulate active composition, comprising a nanoparticulate active agent having effective average particle size prior to incorporation in a solid dose form of less than about 1 micron (0029). The average particle size of less than about 1 micron and upon reconstitution in media representative of human physiological conditions, the solid dose nanoparticulate composition redisperses such that 90% of the active agent particles have a particle size of less than about 5 microns (would reads on 15% fines), and the particle size is measured by conventional particle size measuring techniques well known to those skilled in the art (0042-0043). Additional disclosure includes that the bioavailability of the active drug will increase with redisperse of the active agent into small particle sizes upon administration.

It would have been obvious to one of ordinary skill in the art at the time invention, to incorporate nanoparticulate active agent into compositions of Gowan and Ohta. The person of ordinary skill in the art would have been motivated to make those modification because Ryde teaches that redisperibility properties of a solid dose nanoparticulate formulation prevents the formation of clumps or agglomerated drug particles and there by increases the bioavailability of active agent upon administration. Therefore, one of ordinary sill in the art would have had a reasonable expectation of success because it is well in the art that small particle size (active agent) allows achievement of a given drug plasma concentration at a lower oral dose and the safety profile of the drug can be more accurately controlled because dosing with consistent and defined particle sizes allows for greater reliability in the dosing of the drug necessary to achieve a desired result.

Response to Arguments

Applicant's arguments filed on 01/19/2011 have been fully considered but they are not persuasive.

Applicant argues that Gowan discloses a tablet comprising at least three separate types of particles: taste-masked drug particles, a compressible carbohydrate, and a binder and the binder component is external to the taste-masked drug particles, instead of within the taste-masked drug particle as claimed.

This argument is not persuasive because claims are product-by-process claims, which are not limited to the manipulations of the recited steps, but only the structure implied by the steps. Even though product-by-process claims are limited by

and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even thought the prior product was made by a different process. See In re Thorpe, 777 F.2d 695, 698,227 USPQ 966 (Fed. Cir. 1985). Here, no structural or functional differences are apparent from the process the pharmaceutical tablets are formed because the process used in the prior art dose not formulate microcapsule wherein the drug particles and polymeric binder are granulated to mass, instead, the active pharmaceutical is coated with taste-masked coating, a water-disintegratable, compressible carbohydrate, and a binder. The binder is used to add cohesiveness to the formulation, thereby providing the necessary bonding to form a cohesive mass or compact upon compression. With regards to claims, the resulting product is also a tablet that rapidly disintegrates in the oral cavity comprising drug particles, binders such as cellulosic derivatives, or ethyl cellulose/hydroxypropyl cellulose polymer and others which appears to be the same as when rapidly disintegrating tablets are made.

Applicant argues that Gowan fails to disclose any information regarding friability or levels of fines for the drug particles. This argument is not persuasive since Gowan discloses that the compressed dosage forms, such as tablet, have hardness sufficient to cause the carbohydrate to disintegrate within 30 seconds after oral administration, thereby allowing the coated particles are released from the dosage form with no objectionable taste and swallowed by the user (col. 3 lines 1-7).

Applicant argues that Gowan's formulation does not include the RDMs of the claimed invention. Gowan fails to disclose the disintegrant component of the RDMs.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413,208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091,231 USPQ 375 (Fed. Cir. 1986).

In this case, the Gowan's patent is relied upon to show that it is known in the art to manufacture rapidly disintegrating pharmaceutical dosage forms using conventional techniques containing at least one pharmaceutical particle coated with a taste-maksing composition, a water-disintegratable, compressible carbohydrate and a binder while the Ohta's patent shows an equivalence that is recognized in the art for manufacturing intraorally rapidly disintegratable tablet comprising sugar alcohol or saccaharide having an average particle diameter of not more than 30 microns, and a disintegrant RDM).

Applicant argues that as amended, the claimed invention recite RDMs "consisting essentially of sugar alcohol or saccharide or a mixture thereof and a disintegrant." The granules of Ohta includes the active agent component which is not present in the claimed RDMs- would reasonably be expected to materially affect the basic and novel characteristics of the claimed invention.

This argument is not persuasive because " consisting essentially of' claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir.

1998). See also Atlas Powder v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); In re Janakirama-Rao, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); Water Technologies Corp. vs. Calco, Ltd., 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also AK Steel Corp. v. Sollac, 344 F.3d 1234, 1240-41, 68 USPQ2d 1280, 1283-84 (Fed. Cir. 2003). The Ohta's patent discloses manufacturing intraorally rapidly disintegratable tablet comprising sugar alcohol or saccaharide having an average particle diameter of not more than 30 microns, an active agent and a disintegrant. The presence of active agent does not materially effects taste-masking property of the sugar alcohol or sarccharide. Further, Ohta discloses process of preparing rapidly disintegratable tablet by various techniques well known and within the skill of artisan. Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical field (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Applicant argues that the claimed invention includes at least two types of particles: the taste-masked microcapsules, and RDMs. Even if the granules of Ohta were considered to be taste-masked microcapsules according to the claimed invention (which they are not, as discussed above), Ohta's composition would lack the RDMs of the claimed invention. Conversely, even if the granules of Ohta were considered to be RDMs (which they are not, as discussed above), Ohta's composition would lack the taste-masked microcapsules of the claimed invention.

This argument is not persuasive since this reference is combined for its teachings of knowledge in the art for manufacturing intraorally rapidly disintegratable tablet comprising sugar alcohol or saccaharide having an average particle diameter of not more than 30 microns, and a disintegrant (RDM). If Ohta has taste-masked microcapsules, then rejection would have been a 102(b).

Applicant argues that Guo fails to disclose separate particles which are agglomerates of a sugar alcohol/or saccharide and a disintegrant. The compression coated solid dosage form of Guo is designed to be swallowed whole, and not disintegrate in the oral cavity.

This argument is not persuasive since this reference is combined for its teaching of knowledge in the art for coated solid dosage form of a bitter or unpleasant tasting pharmaceutically active agent such as sumatriptan having advantages (elimination of the bitter taste and unpleasant smell).

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. S./
Examiner, Art Unit 1618

/Jake M. Vu/
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